AR201-13659B

06 March 2002

APPENDIX A

ROBUST SUMMARY FOR BUTANENITRILE, 2,2'-AZOBIS(2-METHYL- (AMBN)

CAS NO. 13472-08-7

06 March 2002

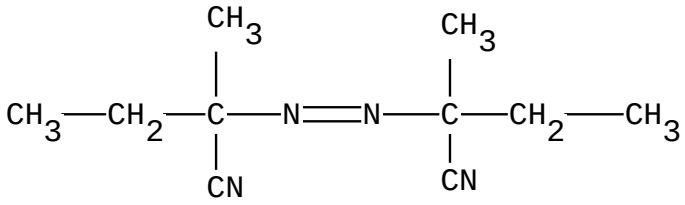
The studies listed below were selected to represent the best available study design and execution for these HPV toxicity endpoints. Other data of equal or lesser quality are not summarized, but are listed as related references in this document.

1.0 Substance Information

CAS Number: 13472-08-7

Chemical Name: Butanenitrile, 2,2'-azobis(2-methyl-

Structural Formula:



Other Names:
2,2'-Azobismethylethylacetonitrile
2,2'-Azobis-2-methylbutyronitrile
2,2'-Asodi(2-methylbutyronitrile)
2,2'-Azobis(2-cyanopentane)
2,2-Azobisisovaleronitrile
2,2'-Azobis(α-methylbutyronitrile)
2,2'-Dimethyl-2,2'-azodibutyronitrile
Azocatalyst M
Azostarter V 59
V 59
Perkadox AMBN
Vazo® 67
Vazo 64-A
Wako V 59

Exposure Limits: 1 mg/m^3, 8-hour TWA and 0.7 mg/m^3, 12-hour TWA: DuPont Acceptable Exposure Limit (AEL)

2.0 Physical – Chemical Properties

2.1 Melting Point

Value:	45°C
Decomposition:	Decomposition can be violent. Rapid decomposition releases nitrogen in potentially sufficient quantities to result in hazardous pressures or oxygen-deficient atmospheres in tightly confined spaces. Decomposition at temperatures above the Self-Accelerating Decomposition Temperature (SADT), 50°C, can be very rapid.
Pressure:	No Data

Method:	Not Available
GLP:	Unknown
Reference:	DuPont Co. (2000). Material Safety Data Sheet No. DU000905 (March 28).
Reliability:	Not assignable because limited study information was available.

Additional References for Melting Point: None Found.

2.2 Boiling Point: Not Applicable.

2.3 Density

Value:	Specific gravity = 1.1; bulk density = 25 lbs/ft^3
Temperature:	No Data
Method:	Not Available
GLP:	Unknown
Results:	No additional data.
Reference:	DuPont Co. (2000). Material Safety Data Sheet No. DU000905 (March 28).
Reliability:	Not assignable because limited study information was available.

Additional Reference for Density:

DuPont Co. (n.d.). Vazo® Polymerization Initiators: Properties, Uses, Storage, and Handling (also cited in TSCA Fiche OTS0000937).

2.4 Vapor Pressure

Value:	Negligible at room temperature.
Temperature:	No Data
Decomposition:	No Data
Method:	Not Available
GLP:	Unknown
Reference:	DuPont Co. (2000). Material Safety Data Sheet No. DU000905 (March 28).
Reliability:	Not assignable because limited study information was available.

Value:	8.9×10^{-2} Pa
Temperature:	25°C
Decomposition:	No Data
Method:	Estimated using the modified Grain method.
GLP:	Not Applicable
Reference:	SRC MPBPWIN v1.40 in EpiWin v3.05.

	Syracuse Research Corporation (MPBPWIN) program estimates the vapor pressure using the modified Grain method. A description of the methodology is detailed in: Lyman, W. J. (1985). In: Environmental Exposure From Chemicals, Volume I, Chapter 2, Neely, W. B. and G. E. Blau (eds.), CRC Press, Inc., Boca Raton, FL.
Reliability:	Estimated value based on accepted model.

Additional Reference for Vapor Pressure: None Found.

2.5 Partition Coefficient (log Kow):

Value:	3.86
Temperature:	No Data
Method:	Modeled. The KOWWIN computer program, version 1.66 from Syracuse Research Corporation, calculates the Log octanol/water partition coefficient (log Kow) of organic chemicals using an atom/fragment contribution method.
GLP:	Not Applicable
Reference:	The methodology is described in the following journal article: Meylan, W. M. and P. H. Howard (1995). J. Pharm. Sci., 84:83-92.
Reliability:	Estimated value based on accepted model.

Additional References for Partition Coefficient: None Found.

2.6 Water Solubility

Value:	< 1 wt% (< 10 g/L)
Temperature:	No Data
pH/pKa:	No Data
Method:	Not Available
GLP:	Unknown
Reference:	DuPont Co. (2000). Material Safety Data Sheet No. DU000905 (March 28).
Reliability:	Not assignable because limited study information was available.

Value:	4.9 mg/L
Temperature:	25°C
pH/pKa:	No Data
Method:	Modeled

GLP: Not Applicable
Reference: WsKow v1.4 in EpiWin v3.05 (SRC Database).

WsKow estimates the water solubility (Wsol) of an organic compound using the compound's log octanol-water partition coefficient (log Kow). The following journal articles describe the estimation methodology:

Meylan, W. M. et al. (1996). Environ. Toxicol. Chem., 15:100-106.

Meylan, W. M. and P. H. Howard (1994). Upgrade of PCGEMS Water Solubility Estimation Method (May 1994 Draft); prepared for Robert S. Boethling, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC; prepared by Syracuse Research Corporation, Environmental Science Center, Syracuse, NY 13210.

Meylan, W. M. and P. H. Howard (1994). Validation of Water Solubility Estimation Methods Using Log Kow for Application in PCGEMS & EPI (Sept 1994, Final Report); prepared for Robert S. Boethling, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, DC; prepared by Syracuse Research Corporation, Environmental Science Center, Syracuse, NY 13210.
Reliability: Estimated value based on accepted model.

Additional Reference for Water Solubility:

DuPont Co. (n.d.). Vazo® Polymerization Initiators: Properties, Uses, Storage, and Handling (also cited in TSCA Fiche OTS0000937).

2.7 Flash Point: Not Applicable.

2.8 Flammability

Results: Flammable limits in air, % by volume: LEL = 0.034 g/L, UEL = Not determined

Autoignition Temperature = 185°C
Method: Not Available
GLP: Unknown
Reference: DuPont Co. (2000). Material Safety Data Sheet No. DU000905 (March 28).

Reliability: Not assignable because limited study information was available.

Additional Reference for Flammability:

DuPont Co. (n.d.). Vazo® Polymerization Initiators: Properties, Uses, Storage, and Handling (also cited in TSCA Fiche OTS0000937).

3.0 Environmental Fate

3.1 Photodegradation

Concentration:	No Data
Temperature:	No Data
Direct Photolysis:	Not Applicable
Indirect Photolysis:	OH Half-life = 3.605 days (12-hour day; concentration of OH radicals =$1.5x10^6$ OH/cm^3).
Breakdown Products:	No Data
Method:	Calculated by AOP Computer Program, Vers. 1.90, Syracuse Research Corporation. The AOP Program, Version 1.90 from Syracuse Research Corporation, estimates the Atmospheric Oxidation Potential. The AOP program estimates the rate constant for the atmospheric, gas-phase reaction between photochemically produced hydroxyl radicals and organic chemicals. The methodology used by the Atmospheric Oxidation Program is based upon the structure-activity relationship (SAR) methods developed by Dr. Roger Atkinson and coworkers (Atkinson et al., 1987; 1995; 1996; 1984). The AOP Program is described in Meylan and Howard, 1993.
GLP:	Not Applicable
Reference:	Atkinson, R. et al. (1987). Intern. J. Chem. Kinet., 19:799-828. Atkinson, R. et al. (1995). Atmos. Environ., 29:1685-1695. Atkinson, R. et al. (1996). Environ. Sci. Technol., 30:329-334. Atkinson, R. et al. (1984). Chem. Rev., 84:437-470. Meylan, W. M. and P. H. Howard (1993). Chemosphere, 26:2293-2299.
Reliability:	Estimated value based on accepted model.

Additional References for Photodegradation: None Found.

3.2 Stability in Water

Concentration:	Not Applicable
Half-life:	Estimated half-life for a model river is 422.9 years.
% Hydrolyzed:	Not Applicable
Method:	The Henry's Law constant for butanenitrile, 2,2'-azobis(2-methyl- (Vazo® 67) is estimated to be $2.19x10^{-10}$ atm-m^3/mole (Henry v3.10 Program, Bond SAR Method in SRC Epiwin v3.05) from its estimated vapor pressure ($6.7x10^{-4}$ mm Hg; MPBPWIN v1.40) and estimated water solubility (4.905 mg/L; WSKOW v1.40). Based on this Henry's Law constant, the estimated volatilization half-life from a model river (1 m deep, flowing 1 m/sec, wind velocity of 5 m/sec) is approximately 422.9 years. The estimated volatilization half-life from a model lake (1 m deep, flowing 0.05 m/sec, wind velocity of 0.5 m/sec) is approximately 4613 years (Epiwin v. 3.05).
GLP:	Not Applicable
Reference:	Syracuse Research Corporation Epiwin Version 3.05.
Reliability:	Estimated value based on accepted model.

Additional References for Stability in Water: None Found.

3.3 Transport (Fugacity)

Media: Air, Water, Soil, Sediment

Distributions:

Compartment	Released 100% to air	Release 100% to water	Release 100% to soil
Air	0.00302%	$1.98x10^{-8}$%	$3.76x10^{-7}$%
Water	6%	98%	3%
Soil	93.7%	0.000614%	96.3%
Sediment	0.0758%	1.2%	0.0449%

Adsorption Coefficient:	Not Applicable
Desorption:	Not Applicable
Volatility:	Not Applicable
Method:	Calculated according to Mackay, Level III, Syracuse Research Corporation Epiwin Version 3.05. Emissions (1000 kg/hr) to air, water, and soil compartments using standard EPA Model defaults.

Data Used:
Molecular Weight: 192.27
Henry's Law Constant: $2.19x10^{-10}$ atm-m^3/mole (model

calculation)
Vapor Pressure: $6.7x10^{-4}$ mm Hg (MPBPWIN v1.40)
Log Kow : 3.86 (KOWWIN v1.66)
Soil Koc : 200.9 (PCKOCWIN v1.66)

GLP: Not Applicable

Reference: Syracuse Research Corporation EPIWIN v3.05 contains a Level III fugacity model. The methodology and programming approach was developed by Dr. Donald Mackay and co-workers which is detailed in:

Mackay, D. (1991). Multimedia Environmental Models; The Fugacity Approach, pp. 67-183, Lewis Publishers, CRC Press.

Mackay, D. et al. (1996). Environ. Toxicol. Chem., 15(9):1618-1626.

Mackay, D. et al. (1996). Environ. Toxicol. Chem., 15(9):1627-1637.

Reliability: Estimated value based on accepted model.

Additional References for Transport (Fugacity): None Found.

3.4 Biodegradation: No Data.

3.5 Bioconcentration

Value: 185.7 (Log BCF = 2.269)

Method: Calculated by BCFWIN Computer Program, Vers. 2.14, Syracuse Research Corporation (based on reference below).

GLP: Not Applicable

Reference: The estimation methodology used by BCFWIN is described in the following document prepared for the U. S. Environmental Protection Agency (OPPT): "Improved Method for Estimating Bioconcentration Factor (BCF) from Octanol-Water Partition Coefficient," SRC TR-97-006 (2^{nd} Update), July 22, 1997; prepared for Robert S. Boethling, EPA-OPPT, Washington, DC; Contract No. 68-D5-0012; prepared by William M. Meylan, Philip H. Howard, Dallas Aronson, Heather Printup, and Sybil Gouchie; Syracuse Research Corp., Environmental Science Center, 6225 Running Ridge Road, North Syracuse, NY 13212.

Reliability: Estimated value based on accepted model.

Additional References for Bioconcentration: None Found.

4.0 Ecotoxicity

4.1 Acute Toxicity to Fish: No Data.

4.2 Acute Toxicity to Invertebrates: No Data.

4.3 Acute Toxicity to Aquatic Plants: No Data.

5.0 Mammalian Toxicity

5.1 Acute Toxicity

Type:	**Acute Oral Toxicity**
Species/Strain:	Rat/Sprague-Dawley CD
Value:	337 mg/kg
Method:	OECD 401; doses administered were 202, 254, 320, and 402 mg/kg.
GLP:	Yes
Test Substance:	Butanenitrile, 2,2'-azobis(2-methyl- (Perkadox AMBN), purity 98.5%
Results:	The incidence of mortality was 0, 0, 50, and 80% at 202, 254, 320, and 402 mg/kg. All mortality occurred by day 2. Clinical signs of toxicity, which were seen in surviving and dead animals at all dose levels, included lethargy, staggered gait, muscle tremor, piloerection, salivation, and hunched posture. The surviving animals had no clinical signs of toxicity by day 6. The gross necropsy of dead animals showed abnormal gastrointestinal contents and a single observation of dark areas on the glandular mucosa of the stomach. There were no significant changes observed in the gross necropsy of surviving animals.
Reference:	Akzo Chemicals International BV (1991). Unpublished Data, "Perkadox AMBN: Acute Oral Toxicity Study In The Rat" (8/5/91).
Reliability:	High because a scientifically defensible and guideline method were used.

Additional Reference for Acute Oral Toxicity:

Data from this additional source supports the study results summarized above. This study was not chosen for detailed summarization because the data were not substantially additive to the database.

DuPont Co. (1978). Unpublished Data, Haskell Laboratory Report No. 577-78.

Type:	**Inhalation ALC**
Species/Strain:	Male rats/Crl:CD®
Exposure Time:	4 hours
Value:	>8.9 mg/L
Method:	Groups of 6 rats (7-8 weeks old) were exposed nose-only for single, 4-hour periods to dust atmospheres of the test substance in air at concentrations of 1.8, 3.7, and 8.9 mg/L (the highest concentration that could be generated). Rats were weighed and observed daily for 14 days post exposure, weekends included when deemed necessary. Dust atmospheres were generated and calibrated volumes of test atmosphere were drawn through pre-weighed glass fiber filters. Atmospheric concentration was determined from filter weight gain. Percent and mass median diameter of respirable particulate were determined during each exposure. Chamber temperature was monitored.
GLP:	No
Test Substance:	Butanenitrile, 2,2'-azobis(2-methyl- (Vazo® 67), purity >98%
Results:	No mortality was observed at any exposure level tested. The % respirable particulates <10 μm was 11, 25 or 31, and 24 at 1.8, 3.7, and 8.9 mg/L, respectively. The % respirable particulates <5 μm was 2.0, 8.2 or 10, and 8.2 at 1.8, 3.7, and 8.9 mg/L, respectively. The mass median diameter of respirable particulate (μm), calculated for particles less than 10 μm, was 6.8 or 7.5, and 5.1 at 3.7 and 8.9 mg/L, respectively. The mass median diameter of respirable particulate for the 1.8 mg/L group could not be calculated. All rats exhibited slight to severe weight loss 1 day post-exposure. At 8.9 mg/L, 1 rat continued to lose weight for 1 more day. Weight loss was followed by normal weight gain. Rats exposed to 1.8 and 3.7 mg/L exhibited red to brown ocular and/or nasal discharge for 1 day post-exposure. No other adverse clinical signs were observed.
Reference:	DuPont Co. (1983). Unpublished Data, Haskell Laboratory Report No. 368-83.
Reliability:	Medium because a suboptimal study design was used. Only a small percentage of particles in the exposure atmospheres were of respirable size.

Additional References for Acute Inhalation Toxicity: None Found.

Type: **Dermal Toxicity:** No Data.

Type:	**Dermal Irritation**
Species/Strain:	Rabbits/New Zealand White
Method:	OECD 404. A 0.5 g sample was applied directly to the skin, and covered by a gauze patch, for a 4-hour exposure period. The control site was covered by a similar semi-occlusive dressing.
GLP:	Yes
Test Substance:	Butanenitrile, 2,2'-azobis(2-methyl- (Perkadox AMBN), purity 98.5%
Results:	There was no irritation seen in any of the three animals used in the study during the 72-hour observation period.
Reference:	Akzo Chemicals International BV (1991). Unpublished Data, "Perkadox AMBN: Acute Dermal Irritation/Corrosion Test In The Rabbit" (7/26/91).
Reliability:	High because a scientifically defensible and guideline method was used.

Additional References for Dermal Irritation:

Data from these additional sources support the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

DuPont Co. (1980). Unpublished Data, Haskell Laboratory Report No. 513-80.

DuPont Co. (1980). Unpublished Data, Haskell Laboratory Report No. 511-80.

Type:	**Dermal Sensitization**
Species/Strain:	Guinea pigs/Duncan Hartley
Method:	The primary irritation test was conducted on 10 guinea pigs by applying 0.05 mL of an 80% and an 8% suspension of the test substance in dimethyl phthalate (DMP) on shaved, intact shoulder skin. The induction phase for sensitization was a series of 4 sacral intradermal injections of 0.1 mL of a 1.0% suspension in DMP, 1 each week beginning 2 days after the test for primary irritation. After a 13-day rest period, the test guinea pigs were challenged for sensitization by applying and lightly rubbing in 0.05 mL of an 80% and an 8% suspension of the test substance in DMP on shaved intact shoulder skin. At the same time 10 unexposed guinea pigs (controls) of the same age received identical topical application. Reactions were observed at 24 and 48 hours.
GLP:	No

Test Substance:	Butanenitrile, 2,2'-azobis(2-methyl- (Vazo® 67), purity 100%
Results:	The test substance caused no irritation on shaved intact skin of guinea pigs at 24 or 48 hours. None of the test guinea pigs showed a sensitization response.
Reference:	DuPont Co. (1980). Unpublished Data, Haskell Laboratory Report No. 511-80.
Reliability:	High because a scientifically defensible or guideline method was used.

Additional References for Dermal Sensitization: None Found.

Type:	**Eye Irritation**
Species/Strain:	Male rabbits/Albino
Method:	The solid test substance (28.4 mg) was placed into the right conjunctival sac of each of 2 male albino rabbits. After 20 seconds, 1 treated eye was washed with tap water for 1 minute. The treated eye of the other rabbit was not washed. Observations of the cornea, iris, and conjunctiva were made with a hand-slit lamp at 1 and 4 hours, and at 1, 2, and 3 days. Fluor-i-strip® stain and a biomicroscope were used at examinations after the day of treatment.
GLP:	No
Test Substance:	Butanenitrile, 2,2'-azobis(2-methyl- (Vazo® 67), purity 100%
Results:	The test substance produced no corneal, iritic, or conjunctival effects at any time when tested in rabbit eyes.
Reference:	DuPont Co. (1980). Unpublished Data, Haskell Laboratory Report No. 514-80.
Reliability:	High because a scientifically defensible or guideline method was used.

Type:	**Eye Irritation**
Species/Strain:	Rabbits/New Zealand White
Method:	OECD 404. A 0.1 g sample was instilled into the right eye of the animals. The left eye was untreated.
GLP:	Yes
Test Substance:	Butanenitrile, 2,2'-azobis(2-methyl- (Perkadox AMBN), purity 98.5%
Results:	There was no irritation seen in any of the three animals used in the study at the 24-hour observation period until the end of the study (72-hour observation period). There was irritation of the conjunctiva and slight chemosis seen in all animals, and iritis seen in two animals at the 1-hour observation period.
Reference:	Akzo Chemicals International BV (1991). Unpublished

	Data, "Perkadox AMBN: Acute Eye Irritation Test In The Rabbit" (8/5/91).
Reliability:	High because a scientifically defensible and guideline method was used.

Additional References for Eye Irritation: None Found.

5.2 Repeated Dose Toxicity: No Data.

5.3 Developmental Toxicity: No Data.

5.4 Reproductive Toxicity: No Data.

5.5 Genetic Toxicity

Type:	***In vitro* Bacterial Reverse Mutation Assay**
Tester Strains:	*Salmonella typhmurium* strains TA98, TA100, TA1535, TA1537
Exogenous Metabolic Activation:	Rat liver S-9
Exposure Concentrations:	50-5000 μg/plate
Method:	OECD 471. Positive controls used were benzo[a]pyrene, 2-nitrofluorene, 2-aminoanthracene, 9-aminoacridine, and sodium azide. The solvent was DMSO.
GLP:	Yes
Test Substance:	Butanenitrile, 2,2'-azobis(2-methyl- (Perkadox AMBN), purity 98.5%
Results:	Negative
Remarks:	No evidence of mutagenic activity was detected, with or without metabolic activation.
Reference:	Akzo Chemicals International BV (1991). Unpublished Data, "Perkadox AMBN: Assessment Of Mutagenic Potential In Histidine Auxotrophs Of *Salmonella Typhimurium* (The Ames Test)" (7/25/91).
Reliability:	High because a scientifically defensible and guideline method was used.

Additional Reference for *In vitro* Bacterial Reverse Mutation Assay:

Data from this additional source support the study results summarized above. This study was not chosen for detailed summarization because the data were not substantially additive to the database.

Takenaka, S. I. et al. (1993). J. Toxicol. Sci., 18(4):418.

Type:	***In vitro* Clastogenicity Studies:** No Data.
Type:	***In vivo* Mouse Micronucleus Assay**
Species/Strain:	Mice/ddY
Sex/Number:	Male
Route of Administration:	Oral
Concentrations:	Not Available
Method:	The micronucleus test using acridine orange staining method was performed in male mice (8-weeks old) following double oral administration.
GLP:	Unknown
Test Substance:	Butanenitrile, 2,2'-azobis(2-methyl-, purity not specified
Results:	Negative
Remarks:	At 24 and 48 hours after treatment, the test substance did not produce a significant increase in the frequency of micronucleated polychromatic erythrocytes in the bone marrow of the treated mice.
Reference:	Takenaka, S. I. et al. (1993). J. Toxicol. Sci., 18(4):418.
Reliability:	Not assignable because limited study information was available.

Additional References for *In vivo* Studies: None Found.

06 March 2002

APPENDIX B

ROBUST SUMMARY FOR PROPANENITRILE, 2,2'-AZOBIS(2-METHYL- (AIBN)

CAS NO. 78-67-1

06 March 2002

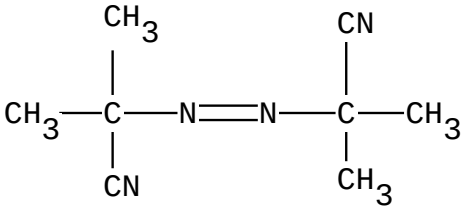
AIBN is exempt from the HPV program because it has already been evaluated through the Organization of Economic Cooperation and Development (OECD) high production volume (HPV) program. A SIDS Initial Assessment Report (SIAR) was prepared for evaluation by the Ninth SIAM convened in France June 29 through July 1, 1999. The studies listed below were selected to represent the best available study design and execution for these HPV toxicity endpoints. Other data of equal or lesser quality are not summarized, but are listed as related references in this document.

1.0 Substance Information

CAS Number: 78-67-1

Chemical Name: Propanenitrile, 2,2'-azobis(2-methyl-

Structural Formula:



Other Names:
Vazo® 64
Alpha, alpha'-azobis(isobutyronitrile)
Alpha,alpha'-azodiisobutyronitrile
Alpha,alpha'-azodiisobutyric acid dinitrile
Azobis(isobutyronitrile)
Azodiisobutyronitrile
Azodiisobutyrodinitrile
2,2'-Azobis(2-methylpropionitrile)
2,2'-Azo-bis(isobutyronitrile)
2,2'-Dicyano-2,2'-azopropane
2,2'-Dimethyl-2,2'-azopropionitrile
Aceto AZIB
Aceto AZDH
Aceto AZDN
AIBN
Genitron®
Genitron® AZDN
Pianofor AN
Porofor N
Porofor-57
Purifier N

Exposure Limits: 1 mg/m^3, 8-hour TWA and 0.7 mg/m^3, 12-hour TWA: DuPont Acceptable Exposure Limit (AEL)

2.0 Physical/Chemical Properties

2.1 Melting Point

Value:	100-103ºC
Decomposition:	No
Sublimation:	No
Pressure:	No Data
Method:	No Data
GLP:	No
Reference:	MITI, JAPAN (n.d.). (cited in OECD SIDS Dossier for 2,2'-Azobis(2-methylpropionitrile), http://www1.oecd.org/ehs/sidstable/index.htm, accessed January 28, 2002).
Reliability:	Not assignable because limited study information was available.

Additional Reference for Melting Point:

DuPont Co. (2000). Material Safety Data Sheet No. B0000109 (March 28).

2.2 Boiling Point: Not Applicable.

2.3 Density

Value:	Specific gravity = ~ 1.1; bulk density = ~25 lbs/ft^3
Temperature:	No Data
Method:	Not Available
GLP:	Unknown
Results:	No additional data.
Reference:	DuPont Co. (2000). Material Safety Data Sheet No. B0000109 (March 28).
Reliability:	Not assignable because limited study information was available.

Additional Reference for Density:

DuPont Co. (n.d.). Vazo® Polymerization Initiators: Properties, Uses, Storage, and Handling (also cited in TSCA Fiche OTS0000937).

2.4 Vapor Pressure

Value:	8.1×10^{-1} Pa
Temperature:	25ºC
Decomposition:	No Data
Method:	OECD Guideline 104

	The purity of the test substance was 99.6%.
GLP:	Yes
Reference:	MITI, JAPAN (n.d.). (cited in OECD SIDS Dossier for 2,2'-Azobis(2-methylpropionitrile), http://www1.oecd.org/ehs/sidstable/index.htm, accessed January 28, 2002).
Reliability:	High because a scientifically defensible or guideline method was used.

Value:	$1.9x10^{-1}$ Pa
Temperature:	25°C
Decomposition:	No Data
Method:	Estimated using the modified Grain method.
GLP:	Not Applicable
Reference:	SRC MPBPWIN v1.40 in EpiWin v3.05. Syracuse Research Corporation (MPBPWIN) program estimates the vapor pressure using the modified Grain method. A description of the methodology is detailed in: Lyman, W. J. (1985). In: Environmental Exposure From Chemicals, Volume I, Chapter 2, Neely, W. B. and G. E. Blau (eds.), CRC Press, Inc., Boca Raton, FL.
Reliability:	Estimated value based on accepted model.

Additional References for Vapor Pressure:

DuPont Co. (2000). Material Safety Data Sheet No. B0000109 (March 28).

2.5 Partition Coefficient (log Kow)

Value:	1.10
Temperature:	25ºC
Method:	OECD Guideline 107; purity of the test substance was 98%.
GLP:	Yes
Reference:	MITI, JAPAN (n.d.). (cited in OECD SIDS Dossier for 2,2'-Azobis(2-methylpropionitrile), http://www1.oecd.org/ehs/sidstable/index.htm, accessed January 28, 2002).
Reliability:	High because a scientifically defensible or guideline method was used.

Additional References for Partition Coefficient (log Kow): None Found.

2.6 Water Solubility

Value:	350 mg/L (slightly soluble)
Temperature:	25ºC
pH/pKa:	No Data
Method:	OECD Guideline 105; purity of the test substance was 99.6%.
GLP:	Yes
Reference:	MITI, JAPAN (n.d.). (cited in OECD SIDS Dossier for 2,2'-Azobis(2-methylpropionitrile), http://www1.oecd.org/ehs/sidstable/index.htm, accessed January 28, 2002).
Reliability:	High because a scientifically defensible or guideline method was used.

Value:	851.1 mg/L
Temperature:	25°C
pH/pKa:	No Data
Method:	Modeled
GLP:	Not Applicable
Reference:	WsKow v1.4 in EpiWin v3.05 (SRC Database).
	WsKow estimates the water solubility (Wsol) of an organic compound using the compound's log octanol-water partition coefficient (log Kow). The following journal article describes the estimation methodology:
	Meylan, W. M. et al. (1996). Environ. Toxicol. Chem., 15:100-106.
Reliability:	Estimated value based on accepted model.

Additional References for Water Solubility:

DuPont Co. (n.d.). Vazo® Polymerization Initiators: Properties, Uses, Storage, and Handling (also cited in TSCA Fiche OTS0000937).

DuPont Co. (2000). Material Safety Data Sheet No. B0000109 (March 28).

2.7 Flash Point: Not Applicable

2.8 Flammability

Results:	Flammable limits in air, % by volume: LEL = 0.02 g/L, UEL = Not determined
	Autoignition Temperature = 295°C

Method:	Not Available
GLP:	Unknown
Reference:	DuPont Co. (2000). Material Safety Data Sheet No. B0000109 (March 28).
Reliability:	Not assignable because limited study information was available.

Additional Reference for Flammability:

DuPont Co. (n.d.). Vazo® Polymerization Initiators: Properties, Uses, Storage, and Handling (also cited in TSCA Fiche OTS0000937).

3.0 Environmental Fate

3.1 Photodegradation:

Concentration:	No Data
Temperature:	No Data
Direct Photolysis:	Not Applicable
Indirect Photolysis:	OH Half-life = 15.99 days (12-hour day; concentration of OH radicals =$1.5x10^6$ OH/cm^3).
Breakdown Products:	No Data
Method:	Calculated by AOP Computer Program, Vers. 1.90, Syracuse Research Corporation. The AOP Program, Version 1.90 from Syracuse Research Corporation, estimates the Atmospheric Oxidation Potential. The AOP program estimates the rate constant for the atmospheric, gas-phase reaction between photochemically produced hydroxyl radicals and organic chemicals. The methodology used by the Atmospheric Oxidation Program is based upon the structure-activity relationship (SAR) methods developed by Dr. Roger Atkinson and coworkers (Atkinson et al., 1987; 1995; 1996; 1984). The AOP Program is described in Meylan and Howard, 1993.
GLP:	Not Applicable
Reference:	Atkinson, R. et al. (1987). Intern. J. Chem. Kinet., 19:799-828. Atkinson, R. et al. (1995). Atmos. Environ., 29:1685-1695. Atkinson, R. et al. (1996). Environ. Sci. Technol., 30:329-334. Atkinson, R. et al. (1984). Chem. Rev., 84:437-470. Meylan, W. M. and P. H. Howard (1993). Chemosphere,

26:2293-2299.
Reliability: Estimated value based on accepted model.

Additional References for Photodegradation: None Found.

3.2 Stability in Water

Concentration: No Data
Half-life: 263 days @ pH 4 and 25ºC
304 days @ pH 7 and 25ºC
210 days @ pH 9 and 25ºC
% Hydrolyzed: No Data
Method: OECD Guideline 111; purity of the test substance was 99.6%.
GLP: Yes
Reference: MITI, JAPAN (n.d.). (cited in OECD SIDS Dossier for 2,2'-Azobis(2-methylpropionitrile), http://www1.oecd.org/ehs/sidstable/index.htm, accessed January 28, 2002).
Reliability: High because a scientifically defensible or guideline method was used.

Additional References for Stability in Water: None Found.

3.3 Transport (Fugacity)

Media: Air, Water, Soil, Sediment
Distributions:

Compartment	Release 100% to air	Release 100% to water	Release 100% to soil
Air	31.0%	0.5%	0.7%
Water	40.9%	98.6%	28.6%
Soil	27.9%	0.5%	70.6%
Sediment	0.2%	0.4%	0.1%

Adsorption Coefficient: No Data
Desorption: No Data
Volatility: No Data
Method: Fugacity Level III
GLP: Not Applicable
Reference: MITI, JAPAN (n.d.). (cited in OECD SIDS Dossier for 2,2'-Azobis(2-methylpropionitrile), http://www1.oecd.org/ehs/sidstable/index.htm, accessed January 28, 2002).
Reliability: Estimated value based on accepted model.

Additional References for Transport (Fugacity): None Found.

3.4 Biodegradation

Value:	Propanenitrile, 2,2'-azobis(2-methyl- (Perkadox AIBN) biodegraded 7% at day 28 (with silica gel). There was no biodegradation at day 20. The biodegradation only slightly increased to about 15% in the prolonged study of approximately 110 days.
Breakdown Products:	Not Applicable
Method:	OECD Guideline 301. Secondary activated sludge was used as the inoculum. The concentration of the test substance used was 0.7 mg/L. The vehicle was dichloromethane.
GLP:	Yes
Reference:	Akzo Nobel Chemicals (n.d.). Unpublished Data, "Biodegradability Of Perkadox AIBN In The Closed Bottle Test."
Reliability:	High because a scientifically defensible and guideline method was used.

Additional Reference for Biodegradation:

Data from this additional source support the study results summarized above. This study was not chosen for detailed summarization because the data were not substantially additive to the database.

MITI, JAPAN (n.d.). (cited in OECD SIDS Dossier for 2,2'-Azobis(2-methylpropionitrile), http://www1.oecd.org/ehs/sidstable/index.htm, accessed January 28, 2002).

3.5 Bioconcentration

Value:	1.403 (Log BCF = 0.147)
Method:	Calculated by BCFWIN Computer Program, Vers. 2.14, Syracuse Research Corporation (based on reference below).
GLP:	Not Applicable
Reference:	The estimation methodology used by BCFWIN is described in the following document prepared for the U. S. Environmental Protection Agency (OPPT): "Improved Method for Estimating Bioconcentration Factor (BCF) from Octanol-Water Partition Coefficient," SRC TR-97-006 (2nd Update), July 22, 1997; prepared for Robert S. Boethling, EPA-OPPT, Washington, DC; Contract No. 68-D5-0012; prepared by William M. Meylan, Philip H. Howard, Dallas Aronson, Heather Printup, and Sybil

	Gouchie; Syracuse Research Corp., Environmental Science Center, 6225 Running Ridge Road, North Syracuse, NY 13212.
Reliability:	Estimated value based on accepted model.

Additional References for Bioconcentration: None Found.

4.0 Ecotoxicity

4.1 Acute Toxicity to Fish

Type:	**96-Hour LC_{50}**
Species:	*Brachydanio rerio* (Zebra fish)
Value:	580 mg/L (based on nominal test concentrations)
Method:	OECD Guideline 203. Fish (7/dose group) were exposed to 62.5, 125, 250, 500, or 1000 mg/L under semi-static conditions. The temperature was 22.5-23.5°C. The oxygen concentrations were 8.6-8.9 mg/L. The pH ranged from 7.9-8.2. The water hardness was 12°dH. The fish had an average size of 3.1 cm and an average weight of 0.31 g.
GLP:	Yes
Test Substance:	Propanenitrile, 2,2'-azobis(2-methyl- (Perkadox AIBN), purity 99.2%
Results:	There were no mortality or signs of toxicity observed at concentrations of 62.5, 125, and 250 mg/L. There was 29% mortality at 500 mg/L and 100% mortality at 1000 mg/L. The NOEC was 250 mg/L.
Reference:	Akzo Nobel Chemicals (1996). Unpublished Data, "Acute Toxicity Of Perkadox AIBN To The Freshwater Fish *Brachydanio Rerio*" (3/21/96).
Reliability:	Medium because a suboptimal study design was used (nominal test concentrations).

Additional References for Acute Toxicity to Fish:

Data from these additional sources support the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

DuPont Co. (1997). Unpublished Data, Haskell Laboratory Report No. 1997-01184.

Environment Agency of Japan (1996). (cited in OECD SIDS Dossier for 2,2'-Azobis(2-methylpropionitrile), http://www1.oecd.org/ehs/sidstable/index.htm, accessed January 28, 2002).

4.2 Acute Toxicity to Invertebrates

Type:	**48-hour EC_{50}**
Species:	*Daphnia magna*
Value:	397 mg/L (95% confidence interval, 195-811 mg/L)
Method:	*Daphnia magna* were exposed to the test substance in a static, acute 48-hour screening test. Nominal concentrations tested were 0, 0.5, 1.0, 50, 500, and 5000 mg/L, with replicate test chambers used at each dose level. Dissolved oxygen and pH were reported at test initiation (0 hours) and test completion (48 hours).
GLP:	No
Test Substance:	Propanenitrile, 2,2'-azobis(2-methyl- (Vazo® 64) purity not specified
Results:	The test substance exhibited slight toxicity in a 48-hour, unaerated, static acute test using *Daphnia magna*. Based on visual observations, the water control solution was clear and had no color, and the 0.5, 1.0, 50, 500, and 5000 mg/L test solutions all had undissolved test material present throughout the test. Immobilities were 0, 0, 0, 0, 60, and 100% at 0, 0.5, 1.0, 50, 500, and 5000 mg/L, respectively. All water quality parameters were within acceptable limits. Dissolved oxygen at test initiation and completion was 8.4 mg/L. The pH ranged from 7.7-7.8 and 7.9-8.2 at test initiation and completion, respectively.
Reference:	DuPont Co. (1997). Unpublished Data, Haskell Laboratory Report No. 1997-01185.
Reliability:	Medium because a suboptimal study design was used (nominal test concentrations).

Additional References for Acute Toxicity to Invertebrates:

Data from these additional sources support the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

Environment Agency of Japan (1995). (cited in OECD SIDS Dossier for 2,2'-Azobis(2-methylpropionitrile), http://www1.oecd.org/ehs/sidstable/index.htm, accessed January 28, 2002).

Service Analyse Environment (France). (cited in OECD SIDS Dossier for 2,2'-Azobis(2-methylpropionitrile), http://www1.oecd.org/ehs/sidstable/index.htm, accessed January 28, 2002).

4.3 Acute Toxicity to Aquatic Plants

Type:	**72-hour EC_{50} Biomass**
Species:	*Selenastrum capricornutum* ATCC 22662
Value:	> 9.4 mg/L
Method:	OECD Guideline 201 (1984) was performed. The EC_{50} value for growth rate (% inhibition) was calculated based on 5 measured concentrations (0.46, 0.71, 2.1, 4.2, and 9.4 mg/L). DMF of 100 mg/L was used as a solubilizer.
GLP:	Yes
Test Substance:	Propanenitrile, 2,2'-azobis(2-methyl-, purity 99.3%
Results:	The NOEC was 4.2 mg/L.
Reference:	Environment Agency of Japan (1996). (cited in OECD SIDS Dossier for 2,2'-Azobis(2-methylpropionitrile), http://www1.oecd.org/ehs/sidstable/index.htm, accessed January 28, 2002).
Reliability:	High because a scientifically defensible or guideline method was used.

Additional References for Acute Toxicity to Aquatic Plants:

Data from this additional source support the study results summarized above. This study was not chosen for detailed summarization because the data were not substantially additive to the database.

Service Analyse Environment (France). (cited in OECD SIDS Dossier for 2,2'-Azobis(2-methylpropionitrile), http://www1.oecd.org/ehs/sidstable/index.htm, accessed January 28, 2002).

5.0 Mammalian Toxicity

5.1 Acute Toxicity

Type:	**Oral LD_{50}**
Species/Strain:	Rats/Sprague Dawley
Value:	360 mg/kg (95% confidence limits, 340-380 mg/kg)
Method:	Male and female Sprague Dawley rats (5/dose level) were given single oral doses of a 10.0% solution-suspension in corn oil at doses of 251, 316, 398, and 501 mg/kg. Clinical signs of toxicity were recorded. Survivors were killed 14 days later and gross autopsy was performed.
GLP:	No
Test Substance:	Propanenitrile, 2,2'-azobis(2-methyl-, purity not specified
Results:	Mortality was 0/5, 1/5, 4/5, and 5/5 at 251, 316, 398, and 501 mg/kg. Mortality occurred in 1 to 5 days, with most deaths within 2 days. Clinical signs of toxicity included reduced appetite and activity (2-3 days in survivors),

	increasing weakness, tremors, collapse, and death. Gross autopsy of animals that died revealed hemorrhagic areas of the lungs and liver, and acute gastrointestinal inflammation. The viscera appeared normal in survivors.
Reference:	Monsanto (1974). Younger Laboratories, Inc. Report No. Y-74-61 (TSCA Fiche OTS0545441).
Reliability:	Medium because a suboptimal study design was used.

Additional References for Acute Oral Toxicity:

Data from these additional sources support the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

DuPont Co. (1962). Unpublished Data, Haskell Laboratory Report No. 27-62 (also cited in TSCA Fiche OTS0546516 and OTS0000937).

DuPont Co. (1947). Unpublished Data, Haskell Laboratory Report No. 25-47.

Budavari, S. et al. (eds.) (1989). The Merck Index. An Encyclopedia of Chemicals, Drugs, and Biologicals, p. 146, Merck & Co., Inc., Rahway, NJ.

Eastman-Kodak Co. (n.d.). Toxicity and Health Hazard Summary (TSCA Fiche OTS0001156).

Eastman Kodak Co. (1960). TSCA Fiche OTS0555369.

Rusin, V. Y. (1958). Tr. Naunchn. Sess. Leningr. Nauchno. – Issled. Inst. Gig. Tr. Profzabol., pp. 247-251.

Type:	**Inhalation LC_{50}**
Species/Strain:	Male and female rats/ Crl:CD®
Exposure Time:	1 hour
Value:	> 7.78 mg/L
Method:	The method was in accordance with the International Maritime Dangerous Code (IMDG code, pg. 6003-1,2). Male and female Crl:CD® rats (10/exposure level) were exposed nose only to the test substance at concentrations of 1.57, 3.40, and 7.78 mg/L. All rats were weighed and observed daily for 2 weeks post-exposure, except for the Saturday and Sunday of the 2nd week post-exposure. At approximately 10-minute intervals, calibrated volumes of test atmospheres were drawn through pre-weighed glass fiber filters, and atmospheric concentrations were determined. Percent respirability (≤10 μm) was determined during each exposure. Percent respirability was 7.96, 10.0,

	and 6.65 at 1.57, 3.40, and 7.78 mg/L, respectively.
GLP:	Yes
Test Substance:	Propanenitrile, 2,2'-azobis(2-methyl- (Vazo® 64), purity >98%
Results:	One male rat died 1 day after exposure to 1.57 mg/L. No other deaths occurred throughout the study. Most rats exhibited moderate to severe weight losses 1 or 2 days after exposure, followed by a return to a normal weight gain rate. Approximately ½ of the rats exhibited wet or stained perineal areas for 1 to 2 days after exposure. Most females exhibited sporadic weight loss during the 2-week observation period. Seven of 10 female rats exposed to 7.78 mg/L had hair loss, mainly around the head, face, and forelegs. No male rats had hairloss at this concentration. Two males and 1 female had back or foreleg hair loss after exposure to 3.40 mg/L; no rats had hair loss after exposure to 1.57 mg/L. During exposures, rats' faces were covered with dust, which was removed from the fur after the exposure. A dried red discharge around the facial area was observed in some rats a day after exposure, but was not considered test substance-related.
Reference:	DuPont Co. (1984). Unpublished Data, Haskell Laboratory Report No. 196-84.
Reliability:	Medium because a suboptimal study design was used. Only a small percentage of particles in the exposure atmospheres were of respirable size.

Additional References for Acute Inhalation Toxicity:

Data from these additional sources support the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

DuPont Co. (1962). Unpublished Data, Haskell Laboratory Report No. 88-62 (also cited in TSCA Fiche OTS0000937).

DuPont Co. (1981). Unpublished Data, Haskell Laboratory Report No. 40-81 (also cited in TSCA Fiche OTS0000937).

Eastman-Kodak Co. (n.d.). Toxicity and Health Hazard Summary (TSCA Fiche OTS0001156).

Type:	**Dermal ALD**
Species/Strain:	Rabbits/New Zealand White
Exposure Time:	24 hours
Value:	5010-7940 mg/kg

Method:	The test substance was applied as a 40.0% solution-suspension in corn oil to the skin of rabbits (1 male or 1 female) for a 24-hour exposure. Survivors were killed 14 days later.
GLP:	No
Test Substance:	Propanenitrile, 2,2'-azobis(2-methyl-, purity not specified
Results:	The animal dosed with 5010 mg/kg survived, while the rabbit dosed with 7940 mg/kg died within 9 days. Clinical signs observed included reduced appetite and activity (4 days in the survivor), increasing weakness, collapse, and death. Gross autopsy of the rabbit that died revealed hemorrhagic areas of the lungs, liver hyperemia, enlarged gall bladder, discolored kidneys, and gastrointestinal inflammation. The viscera of survivors appeared normal.
Reference:	Monsanto (1974). Younger Laboratories, Inc. Report No. Y-74-61 (TSCA Fiche OTS0545441).
Reliability:	Medium because a suboptimal study design was used.

Additional References for Acute Dermal Toxicity:

Data from these additional sources support the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

Eastman-Kodak Co. (n.d.). Toxicity and Health Hazard Summary (TSCA Fiche OTS0001156).

Eastman Kodak Co. (1960). TSCA Fiche OTS0555369.

Rusin, V. Y. (1958). Tr. Naunchn. Sess. Leningr. Nauchno. – Issled. Inst. Gig. Tr. Profzabol., pp. 247-251.

Type:	**Dermal Irritation**
Species/Strain:	Rabbits/New Zealand White
Method:	OECD Guideline No. 404 and EC Guideline 92/69/E.E.C., B_4.
GLP:	Yes
Test Substance:	Propanenitrile, 2,2'-azobis(2-methyl-, purity 99.2%
Results:	The test material was not irritating to rabbit skin.
Reference:	ELF Atochem (1996). Laboratory study number 14350 TSG (cited in OECD SIDS Dossier for 2,2'-Azobis(2-methylpropionitrile), http://www1.oecd.org/ehs/sidstable/index.htm, accessed January 28, 2002).
Reliability:	High because a scientifically defensible or guideline method was used.

Additional References for Dermal Irritation:

Data from these additional sources supports the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

Eastman Kodak Co. (1960). TSCA Fiche OTS0555369.

Monsanto (1974). Younger Laboratories, Inc. Report No. Y-74-61 (TSCA Fiche OTS0545441).

Data from these additional sources were not summarized because it was not the species of choice.

DuPont Co. (1962). Unpublished Data, Haskell Laboratory Report No. 88-62 (also cited in TSCA Fiche OTS0000937).

Eastman-Kodak Co. (n.d.). Toxicity and Health Hazard Summary (TSCA Fiche OTS0001156).

Rusin, V. Y. (1958). Tr. Naunchn. Sess. Leningr. Nauchno. – Issled. Inst. Gig. Tr. Profzabol., pp. 247-251.

Type:	**Dermal Sensitization (MaximizationTest)**
Species/Strain:	Guinea pigs/Duncan Hartley
Method:	OECD Guideline No. 406 and EC Guideline 92/69/E.E.C., B_6.
GLP:	Yes
Test Substance:	Propanenitrile, 2,2'-azobis(2-methyl-, purity 99.2%
Results:	The test substance was not sensitizing to guinea pigs.
Reference:	ELF Atochem (1996). Laboratory study number 14352 TSG (cited in OECD SIDS Dossier for 2,2'-Azobis(2-methylpropionitrile), http://www1.oecd.org/ehs/sidstable/index.htm, accessed January 28, 2002).
Reliability:	High because a scientifically defensible or guideline method was used.

Type:	**Human Patch Test**
Species/Strain:	Human
Method:	Patch testing was performed on 173 humans as described in Kanerva et al., 1988; Estlander, 1990; and Jolanki, 1991, with 2 days occlusion and 3 readings (usually on Days 2, 3, and 4-6). Allergic reactions were scored according to ICDRG recommendations, +, ++, and +++ reactions being

	considered allergic. Irritant reactions were also recorded. Reactions scored as doubtful (?+) or irritant (IR) were classified as irritant.
GLP:	Unknown
Test Substance:	Propanenitrile, 2,2'-azobis(2-methyl-, purity not specified
Results:	At a dose of 1.0% (w/w), the test substance produced no allergic reactions. It produced an irritant reaction in 1 of 173 humans (6%).
Reference:	Kanerva, L. et al. (1997). Contact Dermatitis, 37:301-302.
	Kanerva, L. et al. (1988). Int. Arch. Occup. Environ. Health, 60:89-94.
	Estlander, T. (1990). Acta Dermato-venereologica, Suppl. 155:1-84.
	Jolanki, R. (1991). Acta Dermato-venereologica, Suppl. 155:1-80.
Reliability:	Not assignable because limited study information was available.

Additional References for Dermal Sensitization:

Data from these additional sources support the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

DuPont Co. (1962). Unpublished Data, Haskell Laboratory Report No. 88-62 (also cited in TSCA Fiche OTS0000937).

Eastman-Kodak Co. (n.d.). Toxicity and Health Hazard Summary (TSCA Fiche OTS0001156).

Kanerva, L. et al. (1999). Acta Dermato-Venereologica, 79(4):296-300 (BIOSIS/99/24592).

Type:	**Eye Irritation**
Species/Strain:	Rabbits/New Zealand White
Method:	OECD Guideline No. 405 and EC Guideline 92/69/E.E.C., B_5.
GLP:	Yes
Test Substance:	Propanenitrile, 2,2'-azobis(2-methyl-, purity 99.2%
Results:	The test material was not irritating to the rabbit eye.
Reference:	ELF Atochem (1996). Laboratory study number 14351 TSG (cited in OECD SIDS Dossier for 2,2'-Azobis(2-methylpropionitrile),

	http://www1.oecd.org/ehs/sidstable/index.htm, accessed January 28, 2002).
Reliability:	High because a scientifically defensible or guideline method was used.

Additional References for Eye Irritation:

Data from this additional source was not summarized because the study design was not adequate.

DuPont Co. (1962). Unpublished Data, Haskell Laboratory Report No. 88-62 (also cited in TSCA Fiche OTS0000937).

Data from these additional sources were not summarized because insufficient study information was available.

Eastman-Kodak Co. (n.d.). Toxicity and Health Hazard Summary (TSCA Fiche OTS0001156).

Monsanto (1974). Younger Laboratories, Inc. Report No. Y-74-61 (TSCA Fiche OTS0545441).

5.2 Repeated Dose Toxicity

Type:	**Combined Repeat Dose and Reproductive Toxicity Screening Test**
Species/Strain:	Rats/Crj:CD(SD)
Sex/Number:	Male and female/Number not specified
Exposure Period:	Males: 42 days Females: 14 days before mating to day 3 lactation
Frequency of Treatment:	Daily by gavage
Exposure Levels:	0, 2, 10, and 50 mg/kg/day
Method:	OECD Combined Repeat Dose and Reproductive/Developmental Toxicity Screening Tests Guideline 422.
GLP:	Yes
Test Substance:	Propanenitrile, 2,2'-azobis(2-methyl-, purity, 99.9%
Results:	*Males:* Temporary salivation was induced at ≥10 mg/kg. Decrease in body weight gain and food consumption was observed at 50 mg/kg/day. In the kidneys, absolute and relative weight was increased in all treatment groups, and in ≥ 10 mg/kg/day groups, respectively. In addition, increases in eosinophilic bodies and basophilic changes of the renal tubular epithelial cells were observed in all treatment groups and granular casts in the lower nephrons were observed at

≥ 10 mg/kg/day. As these pathological changes were observed only in males, accumulation of α_{2u}-macroglobulin was suspected as a cause of male specific renal toxicity. Liver weights were significantly increased by 14 and 66% for absolute weight (14 and 74% for relative weight) in the 10 and 50 mg/kg/day group, respectively. Centrilobular hypertrophy of hepatocytes was observed in the 10 and 50 mg/kg/day groups (±: 4 in 13, +:9 in 13 for 10 mg/kg, ++: 13 in 13 for 50 mg/kg, compared to no changes in the 0 and 2 mg/kg groups). In blood analysis, there were several changes at 50 mg/kg, such as an elevation of platelet and white blood cell counts, increases in total protein, albumin, total cholesterol, Ca, and inorganic phosphorus, and decreases in the A/G ratio and Cl concentration.

Females: One animal died on postpartum day 3 at 50 mg/kg/day. Decrease in body weight gain and food consumption was observed at ≥ 10 mg/kg/day. In the kidneys, absolute and relative weights were increased at 50 mg/kg/day. Liver weights were significantly increased by 43% for absolute weight (51% for relative weight) only at 50 mg/kg/day. However, centrilobular hypertrophy of hepatocytes was observed in the 10 and 50 mg/kg/day groups (±: 6 in 13, +: 1 in 13 at 10 mg/kg; ±: 1 in 13, +: 11 in 13, ++: 1 in 13 at 50 mg/kg/day, compared to no changes at 0 and 2 mg/kg/day).

The NOAEL for males and females was 2 mg/kg/day, and the LOAEL for males and females was 10 mg/kg/day.

Reference: MHW, Japan (1997). Ministry of Health and Welfare: Japan, Toxicity Testing Reports of Environmental Chemicals, 5:65 (cited in OECD SIDS Dossier for 2,2'-Azobis(2-methylpropionitrile), http://www1.oecd.org/ehs/sidstable/index.htm, accessed January 28, 2002).

Reliability: High because a scientifically defensible or guideline method was used.

Type: **90-Day Subacute Oral Toxicity**
Species/Strain: Dogs/Purebred beagle
Sex/Number: Male and female/4 per dose
Exposure Period: 90 days
Frequency of Treatment: 7 days/week
Exposure Levels: 0, 50, 150, 300, 1000 ppm
Method: The test substance was incorporated into a stock diet and fed

to dogs 7 days/week. Initially, the body weight of each dog was determined and recorded. Thereafter, weighings were conducted weekly for the duration of the test. Food consumption was recorded. Dogs were examined daily for clinical sings or symptoms indicative of systemic toxicity. Five hematologic, 7 blood chemistry, and 7 urinalysis parameters were measured just prior to the inception of the study, after 42 days, and/or after 85 days for the 0, 50, 150, and 300 ppm groups. The parameters were measured in dogs at 1000 ppm just prior to the inception of the study, and on all surviving dogs after 28 days. At the conclusion of the study, animals were sacrificed and given a complete gross necropsy. Nine organ weights were collected, and representative specimens of approximately 35 organs/tissues were saved for histopathologic examination.

GLP: No

Test Substance: Propanenitrile, 2,2'-azobis(2-methyl-, purity not specified

Results: After the death of 1 animal, the surviving 1000 ppm group animals were sacrificed *in extremis* on Day 28 of the investigation. These animals exhibited body weight losses or no body weight gain, and a reduction in the amount of food consumed during the 4 weeks. The animals were asthenic after 3 weeks on test.

The results of the blood chemistry studies conducted on samples collected from the 1000 ppm animals just prior to sacrifice revealed significant increases in serum alkaline phosphatase, serum glutamic-pyruvic transaminase, and serum glutamic-oxalacetic transaminase activities. The results of the hematologic studies and urinalyses conducted on samples obtained from the 1000 ppm animals revealed no unusual findings. The organ weight and ratio data revealed significant increases in liver and kidney to body weight ratios. Histopathologic examination of a series of tissues from the animals fed 1000 ppm revealed morphologic changes in the liver sections.

No deaths occurred in the 0, 50, 150, or 300 ppm groups. No test substance related findings in body weight/gain, food consumption, or clinical signs were observed at 0, 50, 150, or 300 ppm.

The 300 ppm group animals exhibited an increase in serum alkaline phosphatase activity. The females fed 300 ppm exhibited a slight increase in blood thiocyanate. No test substance-related findings were observed in hematologic or

urinalysis parameters at 300 ppm, nor were there any test substance-related findings in hematologic, blood chemistry, or urinalysis parameters at 50 or 150 ppm.

Marginal increases in liver to body weight ratios were observed at 300 ppm, and in 1 male at 150 ppm. No other organ weight effects were observed. Histopathologic examination revealed test substance-related morphologic changes in the liver of some animals at 150 and 300 ppm. The number of animals with this finding was greater at 300 ppm, but the finding was regarded to be an adaptive response of the liver. No histopathologic findings were observed at 50 ppm.

Reference: Monsanto Co. (1974). Industrial Bio-Test Laboratories, Inc. Report, BTL No. 73-54, IBT No. 651-04494 (TSCA Fiche OTS0545629).

Reliability: High because a scientifically defensible or guideline method was used.

Type: **Subacute Inhalation Toxicity**

Species/Strain: Rats/ Crl:CD®

Sex/Number: Males/10 per concentration level

Exposure Period: 2 weeks

Frequency of Treatment: 6 hours/day, 5 days/week

Exposure Levels: 0, 10.0, 80.0 mg/m^3

Method: Groups of rats were exposed head-only. Five rats/group were randomly selected for sacrifice after the 10th exposure, while the remaining 5 rats/group were sacrificed after a 14-day recovery-observation period. Rats were weighed and observed daily (except weekends) throughout the exposure and recovery period.

Dust atmospheres of the test substance were generated and atmospheric concentration of test substance was determined from weight gain of the filters.

An overnight (16 hour) urine specimen was collected from 10 rats in groups exposed to 0 and 10.0 mg/m^3 and 9 rats exposed to 80.0 mg/m^3 after the 9th exposure. Blood was taken from these rats after the 10th exposure, then 5 rats from the groups exposed to 0 and 10.0 mg/m^3 and 4 rats exposed to 80.0 mg/m^3 were sacrificed for pathological examination. Fourteen days later (recovery), blood and urine samples were collected from the rats remaining in each group. Approximately 12 hematologic parameters were measured or

	calculated. After the 10th exposure, 5 rats from each group were sacrificed for gross and histopathological examination. Remaining rats were sacrificed on the 14th day of recovery for identical follow-up examination. Seven organs were weighed and 22 tissues/organs were saved for histologic evaluation.
GLP:	No
Test Substance:	Propanenitrile, 2,2'-azobis(2-methyl- (Vazo® 64), purity 99%
Results:	The mean TWA concentration was 9.80 and 79.5 mg/m^3 for the 10.0 and 80.0 mg/m^3 design concentrations. Mass median diameter ranged from 8.0-11.5 μ at 80.0 mg/m^3. One rat was sacrificed *in extremis*, following the 4th exposure to 80 mg/m^3. This rat exhibited lung noise, poor righting reflex, stained fur, labored breathing, and sluggishness prior to sacrifice. Pathological examination could not explain the cause of death, however, it was not attributed solely to test substance administration. When compared with controls, rats exposed to 10 mg/m^3 showed a normal rate of weight gain during both the exposure and recovery periods. Mean body weight gain of rats exposed to 80.0 mg/m^3 was significantly reduced on days 2-4 of the exposure period. For the remainder of the test period, these rats exhibited a normal rate of weight gain. No test substance-related clinical signs were noted. All exposed rats tended to have higher serum total proteins than the unexposed controls after 10 exposures. Urine osmolality was lower in rats exposed to 80.0 mg/m^3. Following the 14-day recovery period, no effect was observed in rats at 10.0 mg/m^3, but rats at 80.0 mg/m^3 continued to have higher serum total proteins. No test substance-related pathological lesions occurred in rats exposed to 10.0 mg/m^3. The 80.0 mg/m^3 rats sacrificed after the 10th exposure exhibited a compound-related liver effect, increased cytoplasmic basophilia of hepatocytes. However, this liver effect was not detected in these rats following a 14-day recovery period. The mean relative liver-to-body weight ratios of exposed rats was significantly higher than the control group after exposure 10. This effect was no longer evident after a 14-day recovery period.

Reference:	DuPont Co. (1981). Unpublished Data, Haskell Laboratory Report No. 40-81 (also cited in TSCA Fiche OTS0000937).
Reliability:	High because a scientifically defensible or guideline method was used.

Additional References for Repeated Dose Toxicity:

Data from these additional sources support the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

DuPont Co. (1947). Unpublished Data, Haskell Laboratory Report No. 25-47.

Eastman-Kodak Co. (n.d.). Toxicity and Health Hazard Summary (TSCA Fiche OTS0001156).

Motoc, F. et al. (1971). Arch. Mal. Prof. Med. Trav. Secur. Soc., 32(10-11):653-658 (CA76:122561y).

Preussmann, R. et al. (1969). Ann. N.Y. Acad. Sci., 163(2):697-716 (CA73:12854b).

Boyland, E. and S. Sargent (1951). Br. J. Cancer, 5:433-439.

5.3 Developmental Toxicity: Refer to Reproductive Toxicity Section 5.4 for study following OECD Guideline 422.

5.4 Reproductive Toxicity

Species/Strain:	Rats/Cjr:CD(SD)
Sex/Number:	Male and female/Number not specified
Route of Administration:	Gavage
Exposure Period:	Males: From 14 days before mating to 14 days after mating Females: From 14 days before mating to day 3 of lactation
Frequency of Treatment:	Daily
Exposure Levels:	0, 2, 10, 50 mg/kg
Method:	OECD Combined Repeat Dose and Reproductive/Developmental Toxicity Screening Test Guideline 422
GLP:	Yes
Test Substance:	Propanenitrile, 2,2'-azobis(2-methyl-, purity 99.9%
Results:	There were no adverse effects of the test substance on copulation and fertility, duration of pregnancy, gestation index, or parturition of all treated groups. Three of 12 dams

at 50 mg/kg showed difficulty of nursling, and 2 of them let all their offspring die within the first 4 days after birth. The test substance had no adverse effects on viability, sex ratio, or body weight gain of pups. However, viability of newborns at birth and body weight of nurslings on postnatal day 4 was lower than the control level at 50 mg/kg/day. These changes were considered to be caused by maternal toxicity. There were no morphological abnormalities in pups of any treatment group.

The NOAEL for the parental generation was 10 mg/kg/day. The NOAEL for the F_1 offspring was 50 mg/kg/day.

Reference: MHW, Japan (1997). Ministry of Health and Welfare: Japan, Toxicity Testing Reports of Environmental Chemicals, 5:65 (cited in OECD SIDS Dossier for 2,2'-Azobis(2-methylpropionitrile), http://www1.oecd.org/ehs/sidstable/index.htm, accessed January 28, 2002).

Reliability: High because a scientifically defensible or guideline method was used.

Additional References for Reproductive Toxicity: None Found.

5.5 Genetic Toxicity

Type: ***In vitro*** **Bacterial Reverse Mutation Assay**

Tester Strains: *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537, TA97 (without S9 mix)
Escherichia coli WP2 *uvr*A

Exogenous Metabolic Activation: With and without phenobarbital and 5,6-benzoflavone induced rat liver S9

Exposure Concentrations: With metabolic activation: 0, 313, 625, 1250, 2500, 5000 µg/plate

Without metabolic activation: 0, 313, 625, 1250, 2500, 5000 µg/plate

Method: Guidelines for Screening Mutagenicity Testing of Chemicals (Japan) and OECD Guideline No. 471 and 472. The positive control for tests with metabolic activation was 2-aminoanthracene (5 strains). Positive controls for tests without metabolic activation included sodium azide (TA1535), 9-aminoacridine (TA1537 and TA97), and 2-(2-furyl)-3-(5-nitro-2-furyl) acrylamide (TA100, TA98, and WP2).

GLP: Yes

Test Substance:	Propanenitrile, 2,2'-azobis(2-methyl-, purity 99.9%
Results:	Negative
Remarks:	Toxicity was not observed when tested with or without exogenous metabolic activation. Precipitation was observed at concentrations of 1250 and 2500 μg/plate when tested with and without metabolic activation, respectively. The test substance was negative for induction of mutations when tested with and without metabolic activation.
Reference:	MHW, Japan (1997). Ministry of Health and Welfare: Japan, Toxicity Testing Reports of Environmental Chemicals, 5:65 (cited in OECD SIDS Dossier for 2,2'-Azobis(2-methylpropionitrile), http://www1.oecd.org/ehs/sidstable/index.htm, accessed January 28, 2002).
Reliability:	High because a scientifically defensible or guideline method was used.

Additional References for *In vitro* Bacterial Reverse Mutation Assay:

Data from these additional sources support the study results summarized above. These studies were not chosen for detailed summarization because the data were not substantially additive to the database.

DuPont Co. (1976). Unpublished Data, Haskell Laboratory Report No. 89-76 (also cited in TSCA Fiche OTS0000937).

Eastman-Kodak Co. (n.d.). Toxicity and Health Hazard Summary (TSCA Fiche OTS0001156).

Takenaka, S. et al. (1993). J. Toxicol. Sci., 18(4):418 (Abstract P-223).

Eder, E. et al. (1989). Naunyn-Schmiedeberg's Arch. Pharmacol., 339(Suppl.):R26 (Abstract 102) and Eder, E. et al. (1989). Toxicol. Lett., 48:225-234).

Type:	***In vitro* Chromosomal Aberration Test**
Cell Type:	Chinese hamster lung (CHL/IU) cells
Exogenous Metabolic Activation:	With and without phenobarbital and 5,6-benzoflavone rat liver induced S9
Exposure Concentrations:	0, 0.40, 0.80, 1.6 mg/mL
Method:	Guide for Screening Mutagenicity Testing of Chemicals (Japan) and OECD Guideline No. 473. The short-term treatment was 6 hours, and the continuous treatment was 24 and 48 hours. The positive controls were cyclophosphamide

	and mitomycin for the tests with and without activation, respectively.
GLP:	Yes
Test Substance:	Propanenitrile, 2,2'-azobis(2-methyl-, purity 99.9%
Results:	Negative
Remarks:	Cytotoxicity was not observed. The test substance was negative for clastogenicity and polyploidy when tested both in the presence and absence of metabolic S9 activation.
Reference:	MHW, Japan (1997). Ministry of Health and Welfare: Japan, Toxicity Testing Reports of Environmental Chemicals, 5:65 (cited in OECD SIDS Dossier for 2,2'-Azobis(2-methylpropionitrile), http://www1.oecd.org/ehs/sidstable/index.htm, accessed January 28, 2002).
Reliability:	High because a scientifically defensible or guideline method was used.

Additional References for *In vitro* Clastogenicity: None Found.

Type:	***In vivo* Mouse Micronucleus Assay**
Species/Strain:	Mice/ddY
Sex/Number:	Male/Number not specified
Route of Administration:	Oral
Concentrations:	No Data
Method:	A micronucleus test was performed using groups of male mice orally administered 2 doses of the test substance.
GLP:	Unknown
Test Substance:	Propanenitrile, 2,2'-azobis(2-methyl-, purity not specified
Results:	Negative
Remarks:	At both 24 and 48 hours after treatment, the test substance did not produce a significant increase in the frequency of micronucleated polychromatic erythrocytes in the bone marrow of the treated mice.
Reference:	Takenaka, S. et al. (1993). J. Toxicol. Sci., 18(4):418 (Abstract P-223).
Reliability:	Not assignable because limited study information was available.

Additional References for *In vivo* Genetic Toxicity: None Found.